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Whitcomb

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[54] COMBINATIONS FOR DIABETES

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Related U.S. Application Data

[63] Continuation-in-part of application No. 08/970,057, Nov. 13, 1997, Pat. No. 5,859,037

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[52] **U.S. Cl.** **514/369**; 514/342; 514/593; 514/635; 514/866

[56] References Cited

FOREIGN PATENT DOCUMENTS

0749751 12/1996 European Pat. Off. . 0753298 1/1997 European Pat. Off. . 9609823 4/1996 WIPO .

OTHER PUBLICATIONS

PCT International Search Report, PCT/US97/21996. Oakes, et al., *Diabetes*, vol. 13:1203, 1994, A New Antidiabetic Agent, BRL 49653, Reduces Lipid Availability and Improves Insulin Action and Glucoregulation in the Rat. Hulin, et al, *Current Pharmaceutical Design* 2:85–102, 1996, The Glitazone Family of Antidiabetic Agents.

Groop, M.D., *Diabetes Care*, 15:737–754, 1992, Sulfonylureas in NIDDM.

Nakano, et al., *CS-045*, Clinical Evaluation of a New Oral Hypoglycemic Drug, CS-045, on Daily Profile of Blood Glucose in Patients with Non-Insulin Dependent Diabetes Mellitus (1993).

Company News On–Call, 1–3, 1997 Rezulin® (troglitazone) Receives FDA Marketing Clearance for use as Either Initial or Combination Therapy for Type 2 Diabetes.

Spencer, et al., *Drugs*, vol. 54:89–101, 1997, Troglitazone. Yamasaki, et al., *The Tokohu Journal of Experimental Medicine*, vol. 183:173–183, 1997, Pioglitazone (AD–4833) Ameliorates Insulin Resistance in Patients with NIDDM. Iwamoto, et al., *Diabetic Medicine*, vol. 13:365–370, 1996, Effect of Combination Therapy of Troglitazone and Sulpho-

Effect of Combination Therapy of Troglitazone and Sulphonylureas in Patients with Type 2 Diabetes Who Were Poorly Controlled by Sulphonylurea Alon.

Bressler & Johnson., *Drugs* & *Aging*, vol. 9:418–437, 1996, Oral Antidiabetic Drug Use in the Elderly.

Okaka, et al., *Chemical Abstracts*, vol. 126, No. 20, 1997, Abstract No. 258925, Antidiabetic Effects of Pioglitzone HCL Alone or in Combination with Insulin or Sylfonylurea in Diabetic Animals.

De Souza, et al., *Diabetes*, vol. 44:984–991, 1995, Insulin Secretory Defect in Zucker fa/fa Ratsis Improved by Ameliorating Insulin Resistance.

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[57] ABSTRACT

Combinations of a glitazone antidiabetic agent and a biguanide antidiabetic agent, and optionally a sulfonylurea antidiabetic agent, are useful for treating diabetes mellitus and improving glycemic control.

16 Claims, 12 Drawing Sheets